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Comparative Effectiveness of Sound Therapy, transcranial direct current stimulation, and low-level laser therapy for Chronic Tinnitus Management

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Highlights

- sound therapy, LLLT, and tDCS were assessed for management of chronic tinnitus
- All interventions significantly reduced tinnitus loudness and distress.
- Sound therapy showed the highest clinical improvement in tinnitus symptoms

Abstract

Background and Aim: Tinnitus, the perception of sound without an external source, can significantly impact one's quality of life. Although no definitive cure exists, various treatments aim to reduce symptoms. This study aimed to evaluate the results of the sound therapy, transcranial direct current stimulation (tDCS), and low-level laser therapy (LLLT) in managing chronic tinnitus.

Methods: In a randomized clinical trial, 78 adults with chronic tinnitus and normal hearing were divided into three groups to receive either sound therapy, (tDCS), (LLLT). All participants received treatment over six weeks. Psychoacoustically, we assessed tinnitus pitch, loudness, minimum masking level (MML), and residual inhibition (RI). Loudness and distress were also measured using visual analog scales (VAS), and functional impact was evaluated using the Tinnitus Handicap Inventory (THI) and Tinnitus Functional Index (TFI). Auditory Brainstem Response (ABR) testing was performed to assess neural conduction.

Results: All interventions significantly reduced tinnitus loudness, MML, and distress (p < 0.05). Sound therapy showed the most significant improvements in THI, TFI, and VAS scores. No significant changes were found in ABR latencies. Post-hoc analysis revealed greater benefits in the sound therapy group for THI and TFI compared to the others.

Conclusion: While all approaches showed promise in reducing tinnitus symptoms, sound therapy proved to be the most successful intervention. To improve procedures and investigate customized strategies, more research is required.

Keywords: Tinnitus, sound therapy, transcranial direct current stimulation, low-level laser therapy.

Introduction

Tinnitus, the perception of sound in the absence of an external source, can range from a minor annoyance to a debilitating condition significantly impacting a patient's quality of life [1]. Tinnitus affects people of all ages, but it is more common among those aged 50 to 70. Studies estimate that 10 to 15% of the global adult population experiences tinnitus, and about 20% of those individuals find it bothersome enough to seek treatment [2]. In addition to the auditory symptoms, tinnitus can significantly affect various aspects of well-being, including psychological health, emotional state, sleep patterns, and overall health [3]. Although a definitive cure remains elusive, various treatment options have been developed to manage tinnitus symptoms and improve patients' quality of life. These options include medications, counseling, and several non-invasive neuromodulatory techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) [4]. Despite the range of available treatments, finding a universally effective solution for tinnitus remains a significant challenge. Cognitive Behavioral Therapy (CBT) is a traditional psychological treatment that has confirmed substantial efficiency in reducing tinnitus-related distress by changing maladaptive thought designs and emotional responses. However, CBT was not included in the present study because the objective of this study

was to compare interventions with a direct physiological or neuromodulatory base, such as sound-based and brain stimulation therapies. These methods permit objective and psychoacoustic outcome quantities, which are less seen in CBT. Only participants with tonal, non-pulsatile tinnitus were included in this study. Non-invasive approaches, such as transcranial direct current stimulation, low-level laser therapy, and sound therapy, have shown promise in previous studies [5]. However, research on each therapy is inconsistent, with some studies showing improvements such as reduced tinnitus intensity, improved quality of life, and long-term relief, while others indicate no significant benefit [5]. Importantly, there is a lack of research directly comparing the effectiveness of these therapies for chronic tinnitus. Understanding how these therapies differ is crucial for optimizing treatment strategies. Each therapy targets tinnitus through different mechanisms, and comparing their effects may reveal which treatment is most effective for specific patient profiles or tinnitus characteristics. This study aimed to assess the effectiveness of these treatments in reducing tinnitus symptoms and enhancing the wellbeing of patients with this condition.

There are many studies done on the effect of methods in tinnitus treatment. Yadollahpour et al. [6] reported that tDCS suggestively reduced tinnitus-related distress and loudness in selected patients. Bashir et al. [7] confirmed the potential benefits of low-level laser therapy (LLLT) in reducing tinnitus symptoms, while outcomes varied according to treatment limitations and patient features. Furthermore, Boedts et al. [8] showed sound therapy alone led to clinically significant tinnitus relief after six weeks, confirming its effectiveness in symptom reduction.

In this study, we chose to compare sound therapy, tDCS, and LLLT based on several considerations: 1) All are non-invasive, 2) each has a different proposed mechanism of action—acoustic stimulation, cortical neuromodulation, and peripheral photobiomodulation, respectively, and 3) they are amongst the most studied and clinically employed interventions in tinnitus management. Despite their promise, there is a lack of direct comparison under standardized conditions, which this study aims to report. Various tools are commonly employed to evaluate the severity and impact of tinnitus on patients' lives. Among the most widely used are the Tinnitus Handicap Inventory (THI) and the Tinnitus Functional Index (TFI), both of which are well-validated tools designed to assess the emotional and functional problem of tinnitus [9, 10]. In addition to these self-report measures, Auditory Brainstem Response (ABR) testing has been utilized in research settings to investigate possible neurophysiological changes in individuals with tinnitus, particularly those who present with normal hearing thresholds. Although the ABR has been thoroughly investigated in tinnitus research, inconsistent results have cast doubt on its diagnostic [11]. The aim of the present study was to assess the effectiveness of sound therapy, tDCS, and LLLT in managing chronic tinnitus.

Methods

Participants

Seventy-eight adult men and women with chronic tinnitus were recruited for this randomized controlled trial at an audiology center in a teaching hospital in Baghdad, Iraq. All participants met specific criteria: between the ages of 18 and 55, have a normal hearing threshold (\leq 25 dB HL), have chronic unilateral tinnitus that has persisted for at least six months, and have no history of certain illnesses or drugs, such as Meniere's disease, traumatic brain injury, epilepsy, pregnancy, or cardiac pacemakers. Additionally, they should not have taken ototoxic, antipsychotic, antiepileptic drugs, tricyclic antidepressants, or benzodiazepines within one month before the study. Only patients with unilateral tinnitus are included in the sample size to minimize variability and enhance sample homogeneity. Then, using random allocation software and a block randomization technique, they were randomized to one of three groups, each with 26 participants. Since baseline comparisons can be deceptive and are not regarded as meaningful, statistical testing for them was avoided, as is advised in randomized trials [12]. All patients were explained the process, and their written informed consent was acquired before their involvement in the study. To systematically evaluate changes and treatment effects, all evaluations were carried out once at baseline and once after treatment. Under the Ethical code IR.TUMS.FNM.REC.1402.016, the study was approved by the research ethics committee of Tehran University of Medical Sciences' School of Nursing and Midwifery and Rehabilitation. Iranian Registry of Clinical Trials (IRCT) code is IRCT20111113008082N5.

Outcome measure

Psychoacoustic Tinnitus Assessment

Tinnitus pitch, loudness, and Minimum Masking Level (MML) were assessed using an audiometer (AD226, Interacoustics, Denmark). Tinnitus pitch was determined through a 2AFC procedure across a frequency range of 0.25 to 16 kHz [9]. Participants compared pairs of tones to their tinnitus pitch, selecting the tone that matched it the closest. The tone presentation occurred at a sensation level of 15 dBSPL. Pitch matches were verified by comparison with tones one octave above and below. The intensity of a tone at the tinnitus pitch was progressively increased until it matched the perceived loudness of the tinnitus in order to measure tinnitus loudness. MML was determined similarly, with participants indicating when the presented sound masked their tinnitus. Residual inhibition (RI) was evaluated to assess post-masking tinnitus suppression. After 60 seconds of broadband noise at 10 dB above MML, participants were asked to report any changes in the volume of their tinnitus. Responses were categorized as: 1) tinnitus worsening; 2) no change; 3) partial reduction; or 4) complete suppression. For partial or complete RI, the duration of tinnitus suppression was recorded.

Questionnaires

The study utilized standardized questionnaires, including the Arabic version of the THI [7] and the translated version of the TFI into the Arabic language, to evaluate the impact of tinnitus on daily activities and overall wellbeing. The THI is a 25-item, three-label category scale questionnaire. Patients can be classified into five grades based on a conversion to a 100-point scale: slight (0-16), mild (18-36), moderate (38-56), severe (58-76), and catastrophic (78-100) [9]. TFI is a questionnaire designed to assess tinnitus severity and its negative impact. It employs 25 items (rated 0–10 or 0–100 by increments of 10) to calculate the overall score on a scale of 0–100 (higher generally means more severe) [10]. Additionally, participants assessed their tinnitus loudness and distress using a 10-point Visual Analog Scale (VAS), where 0 indicates no tinnitus and 10 represents tinnitus at its loudest. Tinnitus-related distress was also evaluated on a 10-point VAS, where 0 signifies no distress and 10 reflects a suicidal level of distress [13]. The Clinical Global Impression scale provided a global assessment of tinnitus severity and change after each intervention session. CGI is rated from 1 to 7, where 1 is very much better, 2 is much better, 3 is minimally better, 4 is no change, 5 is minimally worse, 6 is much worse and 7 is very much worse. [14, 15]. To ensure that the effects of treatment could be expressively evaluated, only individuals with a clinically significant level of tinnitus-related distress were included. This is activated as basic grades falling within at least the moderate range on the THI or TFI questionnaires. Participants with minimal or non-distressing tinnitus were excluded from the study.

Electrophysiologic assessment

ABR was conducted to evaluate the brainstem auditory pathways by measuring the latency and amplitude of waves I, III, and V, which provides information about auditory nerve conduction and brainstem function.

ABR recordings were obtained within the first 12 milliseconds using the Eclipse 25 from Interacoustics (Denmark) in a sound-attenuated, electrically shielded room. Participants were positioned supine. Surface electrodes were placed on the scalp: an active electrode on the forehead, a reference electrode on the mastoid of the tested ear, and a ground electrode on the opposite mastoid. For each ear, 1,000 to 2,000 alternating polarity clicks (2-4 kHz, 80 dB hearing level) were delivered at a rate of 12 clicks per second through earphones. Differences in responses between the vertex and the contralateral/ipsilateral mastoid electrodes were recorded, filtered (between 100 and 2,500 Hz), and averaged [10]. Analyzed parameters included the absolute latencies of waves I, III, and V.

Intervention

Sound Therapy Group: Participants used a Microson Free Open In The Canal (ITC) sound generator (Microson, Spain) with Wide Dynamic Range Compression. Devices were programmed based on tinnitus pitch and loudness.

By digitally programming the ITC device, the microphone function was disabled, allowing only the generated noise to serve as the sound source. After loading the pure tone audiometery into the device, the sound generator was programmed, and the noise level provided to the patient was adjusted until it reached an appropriate level that did not exceed the hearing threshold and was inaudible to the patient. Patients were advised to wear the sound generator with tinnitus masking activated for a minimum of eight hours each day over six weeks [16]. Participants were encouraged to use the sound therapy as much as possible, with a goal of eight hours of daily

use. They were required to report their daily usage time online over six weeks. Additionally, the sound generator's usage data could be retrieved by connecting the device to the software, offering an alternative method for tracking usage hours.

Transcranial direct current stimulation group: tDCS was administered using the Neurostim2 device (Medina Teb Gostar Ltd., Iran) across 12 sessions (20 minutes each, twice weekly) [17]. A period of six weeks has been determined for each group (noise therapy and LLLT), and the tDCS sessions are at an average of two sessions per week, so the number was 12 sessions [18].

During each session, a weak electrical current (1 mA) was passed through the scalp using electrodes placed strategically on the head. To ensure patient comfort and gradual adaptation to the stimulation, the intensity of tDCS was not fixed at 1 mA throughout the study. Instead, stimulation began at 1 mA during the first session to minimize discomfort and familiarize participants with the procedure. From the second session onward, the intensity was increased to 2 mA, which was maintained for the remaining sessions, provided the participant tolerated it well. This stepwise increase was implemented to improve patient compliance and avoid early withdrawal due to discomfort. Rubber electrodes (35 cm²) were embedded in saline-soaked (0.85% NaCl) sponges to enhance conductivity and minimize discomfort during stimulation. following the method of Dundas et al. [19]. According to the International 10-20 System's definition of electrode placement, the cathode was positioned over the left dorsolateral prefrontal cortex (DLPFC) (F3) and the anode over the right DLPFC (F4) [17]. Patients were closely monitored during the sessions for any potential side effects, including itching, burning, headaches, or dizziness.

Low-level laser therapy group: The TinniTool EarLaser4 (Switzerland) was used to apply 660 nm wavelength light at 100 mW to the external auditory canal. Treatment consisted of 20 sessions (20 minutes, every other day) over six weeks. The laser probe was aligned horizontally in the canal for optimal exposure [19, 20].

Statistical analysis

Statistical analyses were conducted using SPSS version 19.0 (IBM SPSS Statistics). The Kolmogorov-Smirnov test was employed to assess the normality of data distribution for the psychoacoustic characteristics of tinnitus, questionnaire scores, and ABR waveform latencies. Paired t-tests were performed to compare pre- and post-intervention values for these variables. Additionally, a univariate ANOVA was conducted to examine differences in mean changes of psychoacoustic characteristics and questionnaire scores across intervention sessions. Post-hoc analysis was performed to identify specific group comparisons. Statistical significance was set at a p-value of ≤ 0.05 .

Results

Participant characteristics

The demographic and clinical characteristics of the participants were summarized in Table 1. No significant differences were observed between the three intervention groups in terms of age, gender, tinnitus duration, or baseline values for tinnitus loudness, MML, residual inhibition, THI, TFI, and VAS scores.

All mean differences between groups at baseline were less than 0.2 standard deviations, indicating group homogeneity.

Psychoacoustic tinnitus characteristics

All three interventions significantly reduced tinnitus loudness and MML, as well as a notable increase in the RI (p<0.05) (Table 2). There were no significant differences among the three groups during the interventions for loudness (F(2,75)=1.13, p=0.328), MML (F(2,75)=4.44, p=0.065), and RI (F(2,75)=0.29, p=0.744). These improvements were observed consistently across the post-intervention assessments.

Questionnaires

Tinnitus handicap inventory

All groups demonstrated significant reductions in THI scores after the intervention. The sound therapy group exhibited the most significant decrease in THI scores (mean difference = -13.32 points, 95% CI:-15.41, -11.23; p<0.001) in comparison to tDCS (mean difference=-8.93, 95% CI: -10.78, -7.07; p \leq 0.001 and LLLT (mean difference = -7.67, 95% CI: -10.80, -4.54; p \leq 0.01. ANOVA showed significant differences in THI scores among the groups (F(2,75)=6.35, p=0.003). The sound therapy group experienced the most substantial reduction, followed by the tDCS and LLLT groups. (Figure 1)

Tinnitus functional index

Post-treatment TFI scores declined significantly in all groups. The greatest improvement was observed in the sound therapy group (mean difference = -16.76 points, 95% CI: -21.89, -11.64; p \leq 0.001), tDCS (mean difference = -10.88 points, 95% CI: -13.00, -8.76; p \leq 0.001), and LLLT (mean difference = -7.67 points, 95% CI: -10.80, -4.54; p \leq 0.001), all demonstrated significant differences according to ANOVA (F(2, 75) = 4.03, p=0.022). According to minimum clinically important difference (MCID) estimates ranging from 7.3 to 9.4 points, all interventions exceeded the threshold for clinically meaningful improvement, reinforcing the effectiveness of the applied treatment approaches. A post-hoc analysis by Tukey revealed that the sound therapy group exhibited the most significant improvement (p< 0.05) (Figure 1).

Visual analog scale

VAS scores for loudness (VAS-L) and distress (VAS-A) showed significant reductions in each group after the intervention (see Table 3 for details). ANOVA identified substantial differences in VAS-L and VAS-A scores among the groups (VAS-L: F(2, 75) = 13.83, p<0.001; VAS-A: F(2, 75) = 8.70, p<0.001). Post-hoc Tukey tests revealed that the sound therapy group demonstrated significantly more improvements in both VAS scores compared to the other groups (p<0.05). A comprehensive summary of pre- and post-intervention changes across all outcomes is provided in Table 4.

Clinical global impression

There were no significant differences in CGI scores among the three groups, as determined by ANOVA (F(2, 75)=0.61, p=0.543). All groups showed improvement in global impression scores as reported by the participants.

Electrophysiologic assessment

In contrast to the positive findings from patient-reported tinnitus questionnaires, ABR wave latencies (waves I, III, V, I-III, I-V, and III-V) did not exhibit any statistically significant changes following any of the interventions (sound therapy, tDCS, or LLLT) when compared to pre-intervention measurements or between groups (ANOVA, p>0.05).

Discussion

This study evaluated the effectiveness of three interventions for tinnitus management: sound therapy, transcranial direct current stimulation (tDCS), and low-level laser therapy. All participants demonstrated improvements following treatment, with sound therapy appearing to be the most effective. Improvements were observed in tinnitus loudness, minimum masking level, and residual inhibition time. Additionally, all groups reported reduced tinnitus-related handicap, negative impacts, and distress.

Tinnitus was reduced in this study using a sound generator with built-in masking sounds for a shorter time (8 hours daily for 6 weeks) than Jin et al. [21], who used white noise through an app for a more extended period (3 or 5 hours daily for 3 months). This suggests potential benefits of a more personalized approach using the sound generators, even with shorter treatment times. Another study compared different sound types and discovered that both broadband noise and nature sounds improved tinnitus, with broadband noise having a slight advantage [22]. Although our study did not specifically investigate sound types, future research could investigate their effectiveness within the sound generators. Scherer et al. [23] investigated tinnitus retraining therapy, which combines sound therapy with counseling. While their study showed improvement in all groups regardless of treatment type, it suggests that sound therapy with counseling might not be significantly superior to standard care alone [23]. Our study centered exclusively on sound therapy through the sound generator. Free, open, fully digital, programmable sound generation device, ITC.

Regarding tDCS, we applied stimulation parameters and electrode placement that have previously shown clinical efficacy, resulting in reductions in tinnitus loudness and modulation of cortical activity [24, 25]. Our short-term intensive protocol may offer advantages over the longer-term spaced protocols employed by others [26]. A recent meta-analysis indicates a potential decrease in tinnitus distress for the tDCS group; however, this finding needs further investigation [27]. While some studies show reductions, others do not. Our findings align with those reporting a decrease in loudness [28, 29]. Unlike our study, Pal et al. [26] found no significant improvement using real tDCS compared to sham, highlighting the importance of sham-controlled designs in tinnitus research.

In LLLT, a prior study with a different wavelength (650 nm) and shorter duration (4 weeks) showed no significant improvements compared to our 660 nm and 6 weeks [30]. Another study using a similar laser and schedule (650 nm, 20 minutes daily for three months) reported a decrease in loudness only in the active laser group [31], which aligns with our findings. Our study also noted a significant decrease in MML, a metric that previous research has not explored. Similar to an earlier study [32], our findings indicate reductions in tinnitus handicap across all groups. Both studies suggest a potential sex-based difference, warranting further exploration. According to Engelke et al. [33], the MCID for THI ranges from 7.8 to 12 points. According to Meikle et al. [13], a reduction of \geq 13 points in THI or TFI scores is considered clinically significant. Only the Sound Therapy group achieved reductions in both THI and TFI that surpassed this threshold, indicating clinically meaningful improvement. While the tDCS and LLLT groups also showed statistically significant reductions, they did not reach this level of clinical significance. As all intervention groups in our study exceeded this threshold, our results demonstrate clinically significant improvements in tinnitus-related distress [33].

Sound therapy works by introducing external sounds, which can lead to a perceived relief from tinnitus. It influences brain regions associated with relaxation (precuneus/posterior cingulate cortex), auditory processing (angular gyrus), sensory information processing (thalamus), self-awareness and emotional regulation (inferior frontal gyrus), as well as emotional processing and pain perception (anterior cingulate cortex) [34]. This approach may downregulate tinnitus-related neural activity through habituation and attentional redirection [35].

TDCS sends weak electrical currents to specific brain areas, influencing neuronal activity [36]. It might disrupt ongoing abnormal neural activity associated with tinnitus or promote neuroplastic changes for a sustained reduction [37]. Targeting the DLPFC is thought to reduce tinnitus-related distress by influencing emotional processing and regulation [38]; targeting the anterior cingulate cortex may directly suppress tinnitus perception by modifying neural activity within auditory processing networks. Repeated sessions with proper electrode placement and optimized parameters are crucial [29].

Potential mechanisms of LLLT include enhanced microcirculation, direct cellular stimulation [20], reduced inflammation, and modulation of nerve activity in the auditory pathway [12]. However, evidence for the effectiveness of LLLT remains mixed, underscoring the need for further controlled studies [30].

Limitations

The study's relatively small sample size of 78 participants limits the generalizability of its findings to the larger tinnitus population. Additionally, the six-week intervention period may not be adequate to evaluate long-term treatment outcomes. While including a control group is commendable, the potential placebo effects associated with certain interventions, particularly sound therapy, could introduce confounding variables. Moreover, the use of customized sound therapy presents challenges in standardization, reproducibility, and generalizability, as individual variations complicate comparisons, hinder the broader application of findings, and necessitate advanced calibration that may not always be feasible in clinical settings.

Conclusion

This study provided valuable insights into the effectiveness of sound therapy, tDCS, and LLLT in managing tinnitus. Sound therapy stood out as the most effective intervention in this research; however, all interventions demonstrated promise. Additional research is necessary to optimize treatment protocols, explore personalized approaches, and clarify the underlying mechanisms of action for each intervention. The MCID estimates have been integrated into the results section to underscore the clinical relevance of the observed outcomes.

Ethical Approval: The Research Ethics Committee of the School of Nursing and Midwifery & Rehabilitation, Tehran University of Medical Sciences, granted ethical approval for the study under the ethical code IR.TUMS.FNM.REC.1402.016 (IRCT20111113008082N5).

Availability of Data and Materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declaration

Conflict of interest: The authors declare that they have no conflicts of interest. Author contributions: BAN: Methodology, Investigation, Writing —Original Draft, GM: Supervision, Data Curation, Writing —Review & Editing, NR: Data Analysis, Writing —Original Draft, Visualization. Funding: No external funding was available.

References

- 1. Luxon LM. Tinnitus: its causes, diagnosis, and treatment. BMJ. 1993;306(6891):1490-1. [DOI:10.1136/bmj.306.6891.1490]
- Henry JA, Reavis KM, Griest SE, Thielman EJ, Theodoroff SM, Grush LD, et al. Tinnitus: An Epidemiologic Perspective. Otolaryngol Clin North Am. 2020;53(4):481-99. [DOI:10.1016/j.otc.2020.03.002]
- 3. Bhatt JM, Lin HW, Bhattacharyya N. Prevalence, Severity, Exposures, and Treatment Patterns of Tinnitus in the United States. JAMA Otolaryngol Head Neck Surg. 2016;142(10):959-65. [DOI:10.1001/jamaoto.2016.1700]
- 4. Bae EB, Lee JH, Song JJ. Single-Session of Combined tDCS-TMS May Increase Therapeutic Effects in Subjects With Tinnitus. Front Neurol. 2020;11:160. [DOI:<u>10.3389/fneur.2020.00160]</u>
- 5. Park KW, Kullar P, Malhotra C, Stankovic KM. Current and Emerging Therapies for Chronic Subjective Tinnitus. J Clin Med. 2023;12(20):6555. [DOI:<u>10.3390/jcm12206555</u>]
- Yadollahpour A, Rashidi S, Saki N, Kunwar PS, Mayo-Yáñez M. Repeated Bilateral Transcranial Direct Current Stimulation over Auditory Cortex for Tinnitus Treatment: A Double-Blinded Randomized Controlled Clinical Trial. Brain Sci. 2024;14(4):373. [DOI:10.3390/brainsci14040373]
- Bashir A, Khan N, Rehman AU, Lohana P, Shiblee SA, Asif N. The Effectiveness of Low-Level Laser Therapy in Treating Tinnitus: A Randomized Controlled Trial. Indus Journal of Bioscience Research. 2025;3(4):528-37. [DOI:10.70749/ijbr.v3i4.111]
- Boedts M, Buechner A, Khoo SG, Gjaltema W, Moreels F, Lesinski-Schiedat A, Becker P, MacMahon H, Vixseboxse L, Taghavi R, Lim HH, Lenarz T. Combining sound with tongue stimulation for the treatment of tinnitus: a multi-site single-arm controlled pivotal trial. Nat Commun. 2024 Aug 19;15(1):6806. [DOI:10.1038/s41467-024-50473-z]
- Neff P, Langguth B, Schecklmann M, Hannemann R, Schlee W. Comparing Three Established Methods for Tinnitus Pitch Matching With Respect to Reliability, Matching Duration, and Subjective Satisfaction. Trends Hear. 2019;23:2331216519887247. [DOI:10.1177/2331216519887247]
- 10. Alsarhan HW. Treatment of tinnitus with tinnitus retraining therapy in Iraq. Iraqi J Commun Med. 2012;25(2):179-85.
- Kehrle HM, Granjeiro RC, Sampaio AL, Bezerra R, Almeida VF, Oliveira CA. Comparison of auditory brainstem response results in normal-hearing patients with and without tinnitus. Arch Otolaryngol Head Neck Surg. 2008;134(6):647-51. [DOI:10.1001/archotol.134.6.647]
- 12. Harvey LA. Statistical testing for baseline differences between randomised groups is not meaningful. Spinal Cord. 2018;56(10):919. [DOI:10.1038/s41393-018-0203-y]
- Meikle MB, Henry JA, Griest SE, Stewart BJ, Abrams HB, McArdle R, et al. The tinnitus functional index: development of a new clinical measure for chronic, intrusive tinnitus. Ear Hear. 2012;33(2):153-76. [DOI:10.1097/AUD.0b013e31822f67c0]
- 14. Adamchic I, Langguth B, Hauptmann C, Tass PA. Psychometric evaluation of visual analog scale for the assessment of chronic tinnitus. Am J Audiol. 2012;21(2):215-25. [DOI:10.1044/1059-0889(2012/12-0010)]
- 15. ECDEU Assessment Manual for Psychopharmacology: Publication ADM 76-338. Rockville, MD: National Institute of Mental Health, Psychopharmacology Research Branch; 1976. p. 217-22.
- 16. Hall JW. New handbook of auditory evoked responses. 1st ed. Boston: Pearson; 2007.
- 17. Tyler RS, Perreau A, Powers T, Watts A, Owen R, Ji H, et al. Tinnitus Sound Therapy Trial Shows Effectiveness for Those with Tinnitus. J Am Acad Audiol. 2020;31(1):6-16. [DOI:10.3766/jaaa.18027]
- Shekhawat GS, Vanneste S. Optimization of Transcranial Direct Current Stimulation of Dorsolateral Prefrontal Cortex for Tinnitus: A Non-Linear Dose-Response Effect. Sci Rep. 2018;8(1):8311. [DOI:10.1038/s41598-018-26665-1]

- Dundas JE, Thickbroom GW, Mastaglia FL. Perception of comfort during transcranial DC stimulation: effect of NaCl solution concentration applied to sponge electrodes. Clin Neurophysiol. 2007;118(5):1166-70. [DOI:10.1016/j.clinph.2007.01.010]
- 20. Drviš P, Trotić R, Ries M, Ajduk J, Muslim A, Klančnik M, et al. Low level laser therapy (LLLT) for chronic tinnitus. Laser in Medicine. 2013;1(2):1-5.
- 21. Jin IK, Choi SJ, Ku M, Sim Y, Lee T. The Impact of Daily Hours of Sound Therapy on Tinnitus Relief for People With Chronic Tinnitus: A Randomized Controlled Study. J Speech Lang Hear Res. 2022;65(8):3079-99. [DOI:10.1044/2022_JSLHR-21-00651]
- 22. Durai M, Searchfield GD. A Mixed-Methods Trial of Broad Band Noise and Nature Sounds for Tinnitus Therapy: Group and Individual Responses Modeled under the Adaptation Level Theory of Tinnitus. Front Aging Neurosci. 2017;9:44.
- 23. Tinnitus Retraining Therapy Trial Research Group; Scherer RW, Formby C. Effect of Tinnitus Retraining Therapy vs Standard of Care on Tinnitus-Related Quality of Life: A Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2019;145(7):597-608. [DOI:10.1001/jamaoto.2019.0821]
- 24. Garin P, Gilain C, Van Damme JP, de Fays K, Jamart J, Ossemann M, et al. Short- and long-lasting tinnitus relief induced by transcranial direct current stimulation. J Neurol. 2011;258(11):1940-8. [DOI:10.1007/s00415-011-6037-6]
- 25. Souza DDS, Almeida AA, Andrade SMDS, Machado DGDS, Leitão M, Sanchez TG, et al. Transcranial direct current stimulation improves tinnitus perception and modulates cortical electrical activity in patients with tinnitus: A randomized clinical trial. Neurophysiol Clin. 2020;50(4):289-300. [DOI:10.1016/j.neucli.2020.07.002]
- 26. Pal N, Maire R, Stephan MA, Herrmann FR, Benninger DH. Transcranial Direct Current Stimulation for the Treatment of Chronic Tinnitus: A Randomized Controlled Study. Brain Stimul. 2015;8(6):1101-7. [DOI:10.1016/j.brs.2015.06.014]
- Wang TC, Tyler RS, Chang TY, Chen JC, Lin CD, Chung HK, et al. Effect of Transcranial Direct Current Stimulation in Patients With Tinnitus: A Meta-Analysis and Systematic Review. Ann Otol Rhinol Laryngol. 2018;127(2):79-88. [DOI:10.1177/0003489417744317]
- 28. Vanneste S, De Ridder D. Noninvasive and invasive neuromodulation for the treatment of tinnitus: an overview. Neuromodulation. 2012;15(4):350-60. [DOI:<u>10.1111/j.1525-1403.2012.00447.x</u>]
- 29. Yadollahpour A, Bayat A, Rashidi S, Saki N, Karimi M. Dataset of acute repeated sessions of bifrontal transcranial direct current stimulation for treatment of intractable tinnitus: A randomized controlled trial. Data Brief. 2017;15:40-6. [DOI:10.1016/j.dib.2017.09.006]
- Dehkordi MA, Einolghozati S, Ghasemi SM, Abolbashari S, Meshkat M, Behzad H. Effect of low-level laser therapy in the treatment of cochlear tinnitus: a double-blind, placebo-controlled study. Ear Nose Throat J. 2015;94(1):32-6.
- 31. Teggi R, Bellini C, Piccioni LO, Palonta F, Bussi M. Transmeatal low-level laser therapy for chronic tinnitus with cochlear dysfunction. Audiol Neurootol. 2009;14(2):115-20. [DOI:10.1159/000161235]
- 32. Cuda D, De Caria A. Effectiveness of combined counseling and low-level laser stimulation in the treatment of disturbing chronic tinnitus. Int Tinnitus J. 2008;14(2):175-80.
- Engelke M, Basso L, Langguth B, Zeman F, Schlee W, Schoisswohl S, et al. Estimation of Minimal Clinically Important Difference for Tinnitus Handicap Inventory and Tinnitus Functional Index. Otolaryngol Head Neck Surg. 2025. [DOI:10.1002/ohn.1217]
- 34. Lv H, Liu C, Wang Z, Zhao P, Cheng X, Yang Z, et al. Altered functional connectivity of the thalamus in tinnitus patients is correlated with symptom alleviation after sound therapy. Brain Imaging Behav. 2020;14(6):2668-78. [DOI:<u>10.1007/s11682-019-00218-0</u>]
- Mondelli MFCG, Cabreira AF, Matos IL, Ferreira MC, Rocha AV. Sound Generator: Analysis of the Effectiveness of Noise in the Habituation of Tinnitus. Int Arch Otorhinolaryngol. 2021;25(2):e205-12. [DOI:10.1055/s-0040-1713377]
- 36. Roberts LE, Eggermont JJ, Caspary DM, Shore SE, Melcher JR, Kaltenbach JA. Ringing ears: the neuroscience of tinnitus. J Neurosci. 2010;30(45):14972-9. [DOI:10.1523/JNEUROSCI.4028-10.2010]
- Shekhawat GS, Stinear CM, Searchfield GD. Modulation of Perception or Emotion? A Scoping Review of Tinnitus Neuromodulation Using Transcranial Direct Current Stimulation. Neurorehabil Neural Repair. 2015;29(9):837-46. [DOI:10.1177/1545968314567152]
- 38. Schlee W, Schecklmann M, Lehner A, Kreuzer PM, Vielsmeier V, Poeppl TB, et al. Reduced variability of auditory alpha activity in chronic tinnitus. Neural Plast. 2014;2014:436146. [DOI:10.1155/2014/436146]

Table 1: Baseline	characteristics	of participants
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Characteristics	Sound Therapy	tDCS group	LLLT group		
	group (n=26)	(n=26)	(n=26)		
Female, NO.	10	16	8		
Age, mean \pm SD, y	40.73 ± 10.58	39.35 ± 8.04	41.27 ± 9.38		
Tinnitus duration, NO.					
6-12 m	9	15	15		
13-24 m	11	6	8		
>24 m	6	5	3		
TFI, mean \pm SD	97 ± 19	99 ± 19	105 ± 21		
THI, mean \pm SD	54 ± 9	55 ± 8	55 ± 9		
VASL, mean \pm SD	6 ± 0.90	6 ± 0.86	6 ± 1.15		
VASA, mean \pm SD	7 ± 1.02	7 ± 1.02	8 ± 0.99		
Tinnitus pitch, mean (min-max), Hz	4000 (3000-7000)	4000 (1500-6000)	4000 (1500-6000)		
Tinnitus loudness, mean \pm SD, dBHL	43 ±15	47 ± 14	48 ± 3		
Minimal Masking level, mean ± SD, dBHL	24 ± 6	28 ± 8	20 ± 5		
Residual Inhibition, mean \pm SD, ms	3 ± 1	3 ± 1	3 ± 1		
ABR latency, mean \pm SD, ms					
Wave I	1.89 ± 0.02	1.88 ± 0.01	1.89 ± 0.02		
Wave III	3.91 ± 0.01	3.91 ± 0.02	3.91 ± 0.01		
Wave V	5.89 ± 0.02	5.89 ± 0.03	5.89 ± 0.03		
Wave I -III	2.45 ± 0.03	2.44 ± 0.04	2.44 ± 0.03		
Wave III - V	2.42 ± 0.02	2.42 ± 0.01	2.42 ± 0.01		
Wave I-V	4.58 ± 0.05	4.58 ± 0.05	4.57 ± 0.05		
p-value > 0.05	5				

Table 2: Comparing the psychoacoustic characteristics of tinnitus pre- to post-intervention.

Groups	C	Mean	Std. Deviation	Interva	nfidence al of the rence	t	df	Sig. (2- tailed)
				Lower	Upper			
Sound	loudness	-1.30	0.88	-1.66	-0.95	-7.54	25	0.000
Sound Therapy	MML	-0.20	1.02	0.15	0.21	-1.01	25	0.022
	RI	0.34	0.48	0.15	0.54	3.63	25	0.001
tDCS	loudness	-1.03	0.77	-1.35	-0.72	-6.84	25	0.000
	MML	-1.58	3.06	-2.82	-0.35	-2.64	25	0.014
	RI	0.46	0.58	.227	0.69	4.04	25	0.000
LLLT	loudness	-1.00	0.74	-1.30	-0.69	-6.81	25	0.000
	MML	-0.23	0.77	.54	0.98	-1.51	25	0.003
	RI	0.42	0.57	.19	0.65	3.73	25	0.001

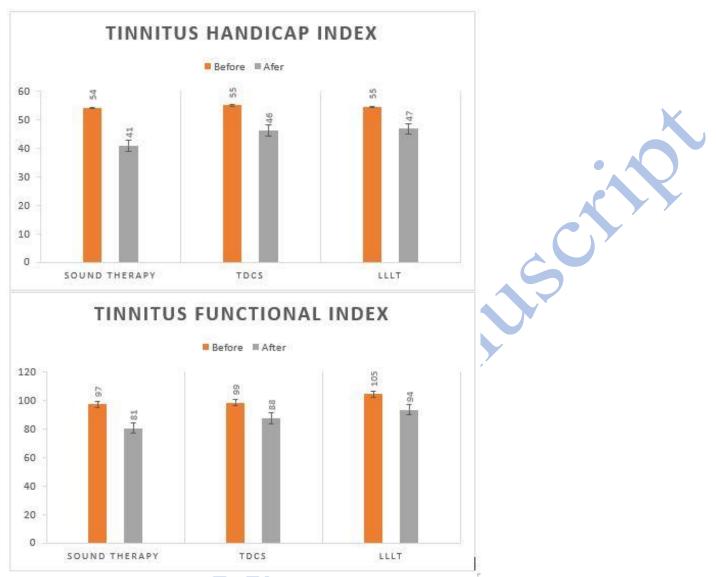


Figure 1: Change in TFI and THI following intervention with error bars represented the standard error.

Table 3: Comparison of visual analog scale pre- to post-intervention.

Groups		Mean of change	Std. Deviation	Interva	nfidence al of the rence	t	df	Sig. (2- tailed)
				Lower	Upper			
Sound therapy	VASL	-2.91	1.56	-3.54	-2.28	-9.52	25	0.000
	VASA	-2.26	1.06	-2.69	-1.83	-10.80	25	0.000
tDCS	VASL	-1.54	1.05	-1.97	-1.11	-7.45	25	0.001
	VASA	-1.80	1.17	-2.27	-1.32	-7.86	25	0.001
LLLT	VASL	-1.54	1.05	-1.97	-1.11	-7.45	25	0.000
	VASA	-1.80	1.17	-2.27	-1.33	-7.86	25	0.000

 Table 4. Pre-post comparison of tinnitus characteristics (psychoacoustic & subjective outcomes)

Group	Measure	Mean Change	SD	95% CI (Lower– Upper)	Т	df	p- value	
Sound Therapy	Loudness	-1.30	0.88	-1.66 to -0.95	-7.54	25	0.000	
Sound Therapy	MML	-0.20	1.02	0.15 to 0.21	-1.01	25	0.022	
Sound Therapy	RI	0.34	0.48	0.15 to 0.54	3.63	25	0.001	
Sound Therapy	VAS-L	-2.91	1.56	-3.54 to -2.28	-9.52	25	0.000	
Sound Therapy	VAS-A	-2.26	1.06	-2.69 to -1.83	-10.80	25	0.000	
tDCS	Loudness	-1.03	0.77	-1.35 to -0.72	-6.84	25	0.000	
tDCS	MML	-1.58	3.06	-2.82 to -0.35	-2.64	25	0.014	
tDCS	RI	0.46	0.58	0.227 to 0.69	4.04	25	0.000	
tDCS	VAS-L	-1.54	1.05	-1.97 to -1.11	-7.45	25	0.001	
tDCS	VAS-A	-1.80	1.17	-2.27 to -1.32	-7.86	25	0.001	
LLLT	Loudness	-1.00	0.74	-1.30 to -0.69	-6.81	25	0.000	
LLLT	MML	-0.23	0.77	0.98 to -1.51	-2.05	25	0.003	
LLLT	RI	0.42	0.57	0.19 to 0.65	3.73	25	0.001	
LLLT	VAS-L	-1.54	1.05	-1.97 to -1.11	-7.45	25	0.000	
LLLT	VAS-A	-1.80	1.17	-2.27 to -1.33	-7.86	25	0.000	

SD = Standard Deviation, CI = Confidence Interval.

Abbreviations

LLLT: low-level laser therapy tDCS: transcranial direct current stimulation TFI: Tinnitus Functional Index THI: Tinnitus Handicap Inventory MML: Minimum Masking Level VAS: Visual analog scale VAS-L: Visual analog scale for loudness VAS- A: Visual analog scale for distress RI: Residual Inhibition

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